

Appl. No. : 09/463,075
Filed : January 14, 2000

- Event
- (b) determining the order of said plurality of genomic DNA fragments in the genome;
- (c) sequencing selected regions of said plurality of genomic DNA fragments;
- and
- (d) identifying nucleotides in said selected regions which vary between individuals, thereby defining a set of single nucleotide polymorphisms; wherein said plurality of single nucleotide polymorphisms comprises single nucleotide polymorphisms having a heterozygosity rate of at least about 0.18 and having a mean inter-marker spacing of less than 50kb.

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88. (Amended) The method of Claim 86, further comprising identifying one single nucleotide polymorphism per genomic DNA fragment.

89. (Amended) The method of Claim 86, further comprising identifying two or more single nucleotide polymorphisms per genomic DNA fragment.

92. (Amended) The method of Claim 86, further comprising selecting single nucleotide polymorphisms having a heterozygosity rate of about 0.32.

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93. (Amended) The method of Claim 86, further comprising selecting single nucleotide polymorphisms having a heterozygosity rate of about 0.42.

94. (Amended) The method of Claim 86, wherein said identifying step comprises identifying at least 20,000 single nucleotide polymorphisms.

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97. (Amended) The method of Claim 86, further comprising determining the position of said single nucleotide polymorphisms along the genome or a portion of the genome.

98. (Amended) The method of Claim 86, further comprising obtaining pluralities of single nucleotide polymorphisms such that each single nucleotide polymorphism is in linkage disequilibrium with at least one of said identified single nucleotide polymorphism.

102. (Amended) The method of Claim 86, further comprising the step of identifying one or more groups of single nucleotide polymorphisms which are in linkage disequilibrium with one another.

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103. (Amended) The method of Claim 86, further comprising the step of identifying one or more groups of single nucleotide polymorphisms wherein the single nucleotide

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polymorphisms in each of these groups are located within a genomic region spanning from 1 to 5kb.

104. (Amended) The method of Claim 86, further comprising the step of identifying one or more groups of single nucleotide polymorphisms wherein the single nucleotide polymorphisms in each of these groups are located within a genomic region spanning from 50 to 150kb.

C. Hart 105. (Amended) The method of Claim 86, further comprising the step of identifying one or more groups of single nucleotide polymorphisms wherein the single nucleotide polymorphisms in each of these groups are located within a genomic region spanning more than 1Mb.

REMARKS

I. Telephonic Interviews

Applicants thank the Examiner for extending the courtesy of telephone interviews on and February 28, 2001 and March 29, 2001 during which the rejections asserted in the Office Action mailed January 10, 2001 were discussed. The substance of these interviews is reflected in the interview summary mailed March 29, 2001 and the remarks below.

Applicants note that in the interview summary mailed March 29, 2001, the Examiner stated "Mr. Hart stressed that the application of technology used in a 2MB sequence to that of a complete human genome is a straightforward issue of scaling." Applicants wish to clarify that armed with the technique disclosed in the present specification one skilled in the art can readily apply the techniques described in the present specification to the entire human genome, and that the demonstration in Example 15 of the specification of the application of the methods of the present invention to a 2Mb sequence is applicable to large regions, including entire chromosomes and the entire human genome. That this is possible to such a large scale can be seen from the body of evidence accumulated by Applicants in their large-region mapping and SNP identification projects, wherein various regions and chromosomes have been mapped and SNPs have been generated. Applicants are proceeding towards a genome wide SNP map of the human genome and have successfully ordered genomic DNA fragments covering large regions of the genome. On the basis of these ordered fragments, Applicants have mapped large regions of the